

### **REMARKS**

In view of the above amendments and following remarks, reconsideration of the rejections contained in the Office Action of July 29, 2005 is respectfully requested.

#### **REJECTION UNDER 35 U.S.C. § 112**

Claim 18 has been amended to address the formality raised by the Examiner in section 4 on page 7 of the Office Action.

#### **REJECTION BASED ON PRIOR ART**

In the Office Action, the Examiner again rejected the claims based upon Japanese Patent Publication No. 7-59812 to Koken Co., Ltd. (Koken) when taken in view of GB Patent No. 1 292 326 to Pichon et al. (Pichon) and WO 99/13902 to Integra Lifesciences Corporation (Integra). However, it is respectfully submitted that the references cited by the Examiner, whether considered individually or taken in consideration of each other, clearly fail to present a prima facie case of obviousness of the present invention. More specifically, they clearly fail to disclose or suggest steps that are clearly set forth in independent claims 1 and 34.

Both independent claims 1 and 34 are directed to a method of preparing a collagen sponge. They both include a step of preparing a collagen gel. Further, they both include a step of mixing air into the collagen gel so as to obtain a collagen foam. Further, they both include a step of drying the collagen foam so as to obtain a dry block of collagen sponge having a three-dimensional structure with stacked chambers which are separated and substantially totally enclosed by walls of collagen material. Each of the claims then further includes a step of isolating, from the block of collagen sponge, parts of the sponge that have certain innominate enumerated properties. With both independent claims, these enumerated properties include a chamber diameter of more than 0.75mm and less than 4mm.

The principally cited reference to Koken has been previously discussed. However, it will be discussed in more detail at this point so as to make it clear how it fails to address the present invention.

In the present invention as claimed in both independent claims 1 and 34, the chambers that result in the collagen sponge are formed by the recited steps of mixing air into the collagen gel so as to obtain a collagen foam and then drying the collagen foam. Koken has no step of mixing air into a collagen gel so as to obtain a collagen foam.

Looking at the cited translation of Koken, Koken does discuss air bubbles communicating straight from one surface to the other surface. However, the air bubbles which Koken discusses are through channels and are the result of the method of Koken, but there is no step of mixing air. Koken is in fact differentiating itself from the prior art use of air bubbles. Note the discussion of the prior art beginning toward the bottom of page 2 of Koken. It identifies a problem in the prior art that “in the case of simply freeze-drying a collagen solution for the method of producing a collagen sponge body, independent air bubbles are only formed randomly, thereby making it difficult to obtain a form that is suitable for use as a wound cover material.”

Koken then goes on to discuss the possibility of using an ammonia gas. The detailed discussion of the invention begins at the top of page 4. Again, where air bubbles are discussed, these air bubbles are a reference to the through-channels that are being produced in Koken, and not to the process of producing them. Rather, the basic formation processes described on page 4 of Koken is “forming a gelatinous body in which straight water columns are formed from one surface to the other surface simultaneous to neutralization of collagen by exposing an acidic solution of collagen to ammonia gas, and subsequently volatilizing the moisture inside the gel by freeze-drying.” Noting the bottom of page 4, “collagen solution is brought close to the isoelectric point of collagen by exposing to ammonia gas, the collagen is neutralized to a gel, the moisture is separated into cylindrical water columns in the collagen, and by freeze-drying this moisture, a collagen sponge is formed that has air bubbles present in a straight line from one surface (top surface layer) to the other surface (back surface layer) that are also substantially independent of each other.” In other words, there is no step of mixing air into a collagen gel so as to obtain a collagen foam as required by claims 1 and 34. Rather, Koken is directed to the process where the moisture is separated into the cylindrical water columns in the collagen to create the through-channels from the top to the bottom of the resulting sponge.

As described at the middle of page 5, the method of Koken involves having an acidic collagen solution, which is without air bubbles, neutralized by exposing it to ammonia gas. There is no discussion or suggestion of ammonia gas being actively mixed into the collagen solution or bubbled through the collagen solution. As described at the middle of page 5, when the collagen acidic solution is exposed to the ammonia gas, the collagen precipitates into fibers extending straight from one surface to the other surface, the solution becomes turbid and the moisture separates into the water columns. Note for example the description of the first embodiment. Trays of the collagen solution are placed into a container. In the container, 30ml of aqueous ammonia in a 50ml container is additionally placed and allowed to stand for 12 hours. There is no disclosure or suggestion of any active mixing or bubbling. Rather, it simply appears that the collagen is exposed to the ammonia gas. The remaining embodiments do not appear any different in this respect.

Accordingly, it is respectfully submitted to be clear that Koken does not disclose or suggest mixing air into the collagen so as to obtain collagen foam. Indeed, doing so would be specifically against the method that is being taught by Koken, i.e., the method of exposing the collagen gel to the presence of ammonia.

As noted above, both independent claims 1 and 34 require that the drying of the collagen foam obtains a dry block of collagen sponge which has a three-dimensional structure with stacked chambers which are separated and substantially totally enclosed by walls of collagen material. As discussed in the description of the present invention on lines 26-29 of page 4, it is an object of the invention to prepare a collagen sponge which is air and liquid tight in the sense that, once the collagen sponge is applied to a wound, it will not allow air or liquid to soak through the collagen sponge. This is achieved by the chambers of the collagen sponge being stacked and substantially totally enclosed by walls of collagen material as recited in the independent claims.

The so-called air bubbles of Koken are open, cylindrical channels that extend completely from the top surface to the bottom surface of the collagen sponge. Accordingly, they cannot be considered to be substantially totally enclosed by walls of collagen material.

Indeed, it appears that stacked chambers that are separated and substantially totally enclosed by walls of collagen material would be against the teachings of Koken. Koken desires that the air bubbles communicate straight from one surface to the other surface to facilitate the exudation of exudate from inside the body, for example, from a wound surface, to provide for rapid healing. Note the recited purpose in Koken.

Accordingly, it becomes clear that the Koken does not provide any evidence to establish a prima facie case of obviousness of the present invention. In the sentence spanning pages 3 and 4 of the Office Action, the Examiner states that it is within the level of skill in the art from Koken to control the diameter of the air bubbles by regulating the amount of collagen and concentration of ammonia gas, thereby making it possible to change the pore size of the collagen sponge. The Examiner thus concludes that “the step of mixing air into collagen gel is expected to result a collagen sponge which has three-dimensional structure with stacked chambers separated and substantially totally enclosed by walls of collagen material.” However, the reference to Koken does not support the Examiner’s conclusion. There is no step of mixing air into a collagen gel in Koken. It is not inherent from Koken to result in a three-dimensional structure with stacked chambers that are separated and substantially totally enclosed by walls of collagen material. As discussed above, Koken forms the collagen sponge in a different way, without the mixing of air, but by exposure to ammonia and subsequent freeze-drying. This results, in Koken, in the open through-channels, called air bubbles in Koken, that extend all the way from one surface to the other. This aspect of the present invention thus cannot be inherent from Koken.

The Examiner’s reference to lines 17-20 of the present application is a reference to Applicant’s description of its invention. There is no admission contained in the section referenced by the Examiner that a step of mixing air into a collagen gel followed by drying of the collagen foam that results in obtaining a dry block of collagen sponge having a three dimensional

structure with stacked chambers which are separated and substantially totally enclosed by walls of collagen material is within the prior art.

The reference to Pichon is directed to a method and apparatus for the preparation of collagen dispersions. It discusses both the possibility of the elimination of air in a dispersion or a gel of collagen, and also discusses the possibility of the inclusion of air. However, it does not render obvious the mixing of air into the collagen material of Koken, because this would be against the teachings of Koken. The mechanism of forming the through channels in Koken is incompatible with the mixing of air into the collagen gel to form a foam as required by claims 1 and 34.

Integra, the PCT reference, is directed to a product for promoting dural or meningeal tissue growth comprising collagen. The object of Integra is to provide a mass-marketable collagen-base dural substitute that would be physiologically compatible to prevent the transmission of viruses and prions to dural substitute recipients. It does not disclose or suggest the step of mixing air into a collagen gel, which would in any case not be obvious in Koken. Nor does it disclose or suggest chambers that are stacked and substantially totally enclosed by the collagen material as recited in claims 1 and 34.

It is respectfully submitted and believed that the above discussion with respect to Koken should make it clear that the independent claims are not disclosed or suggested thereby. Koken is simply incompatible with the method of the present invention as claimed in claims 1 and 34.

Accordingly, further discussion of what may or may not be taught by the secondary references to Pichon and Integra does not appear to be necessary at this point. Nonetheless, Applicant reserves all rights to traverse the various positions taken by the Examiner with respect to such secondary references, as well as their suitability in any obviousness combination.

Should the Examiner disagree with Applicant's position with respect to what is in fact taught by Koken, the Examiner is respectfully requested to contact Applicant's undersigned

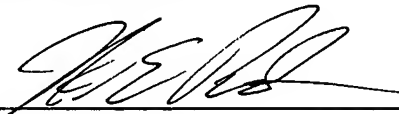
representative for the purpose of setting up an interview to discuss the reference and its teachings.

In view of the above amendments and remarks, it is submitted that the present application is now in condition for allowance, and the Examiner is requested to pass the case to issue. If the Examiner should have any comments or suggestions to help speed the prosecution of this application, the Examiner is requested to contact Applicant's undersigned representative.

Respectfully submitted,

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By: \_\_\_\_\_



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